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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/899,303	07/06/2001	Geert Maertens	BJS-2551-109	3515

23117 7590 11/22/2006

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 11/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/899,303	MAERTENS ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *69,70,73,74,76,87-90,95-97 and 102* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *69,70,73,74,76,87-90 and 102* is/are rejected.

7)☒ Claim(s) *95-97* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

This is to acknowledge the amendment filed on 09/08/2006. Claims 73-74, 96 have been amended. Claim 68 has been canceled. Claims 69-70, 73, 74, 76, 87-90, 95-97 and 102 are pending.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 102

1. Claims 76 and 87 are still rejected under 35 U.S.C. 102(b) as being anticipated by Hsu et al. (Hepatology, May 1993, Vol. 17, No. 5, pp. 763-771) on the same ground as stated in the previous office action.

2. Applicants traverse the rejection and submit that applicants could not find content disclosed by Hsu et al. that teaches the claimed invention cited by examiner in the pervious office action against the claims. On the other hand, applicants admit that the recombinant baculovirus HCV-Bac 3 taught by Hsu is the vector expressing the HCV E1 protein from amino acid residues 133 to 316, wherein the glycocylation site at the 325 is not contained in the polypeptide. However, applicants still argue that the E1 polypeptide taught by Hsu et al. is still different from the claimed E1 glycoprotein because the E1 polypeptide cited in claim 76 has at least one glycosylation being removed at the nucleic acid level.

3. Applicants' argument has been respectfully considered; however, it is not found persuasive. The claimed invention is drawn to a recombinant vector expressing HCV E1 envelope protein E1, which starts in between the amino acid residues 1-192 and ends with 250-400 with at least one glycosylation site present said E1 removed at the nucleic acid level. A reasonable interpretation of the broadest scope of "at least one glycosylation site" cited in claim 76 still includes removal of one glycosylation site at the nucleic acid level. On pages 764 to 765, especially illustrated in Fig. 1, Hsu et al. clearly teach that a recombinant baculovirus vector, i.e.

HCV-Bac 3, comprises the HCV E1 DNA sequence from nucleotides 400 to 950 encoding the amino acid residues from about 133 to 316 (HCV-Bac 3) and the glycosilation site located after the amino acid residue 256 is removed by deletion the nucleic acids encoding said amino acid residue (Please see pages 764-765 and Fig. 1). To this context, the reference by Hsu et al. still anticipates claims 76 and 87.

New ground rejections:

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 69-70, 73, 74, 76, 87-90 and 102 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hsu et al. (Hepatology, May 1993, Vol. 17, No. 5, pp. 763-771) in view of the disclosures by Ralston et al. (WO 92/08734A1), Tartaglia et al. (Virol. 1992, Vol. 188 (1), pp. 217-232), Sutter et al.(Proc. Natl. Acad. Sci. USA. 1992, Vol. 89, pp. 10847-10851) and Vanderbroeck et al. (Eur. J. Biochem. 1993, Vol. 217, pp. 45-52).

6. The claimed invention is drawn to a recombinant vector, preferably a vaccinia viral vector, more preferably vaccina avipox vector or Ankara Modified virus (AMV) vector, which expresses HCV E1 envelope protein E1 starting in between the amino acid residues 1-192 or 117-192 and ending in between 250-400 with at least one glycosylation site remval at the nucleic acid level or in between 285-326.

7. On pages 764 to 765, especially illustrated by Fig. 1, Hsu et al. clear teach that a recombinant baculovirus vector, i.e. HCV-Bac 3, comprises the HCV E1 DNA sequence from nucleotides 400 to 950 encoding the amino acid residues from about 133 to 316 (HCV-Bac 3) and the glycosilation site located after amino acid residue 256 is removed by deletion at the

nucleic acid level. Hsu et al. also teach that the vector is a live recombinant viral vector being able to express said recombinant protein after said viral vector is transfected into SF-9 cells (Please see pages 764-765 and Fig. 1). Hsu et al. do not teach to use vaccinia viral vector, preferably avipox or Ankkara Modified virus (AMV) to express the E1 truncate polypeptide.

8. However, vaccinia viral vector is a well accepted viral vector used for expressing HCV envelope protein E1 or its fragment thereof as evidenced by Ralston et al. Ralston et al. teach a method for expressing HCV envelope protein E1, wherein the HCV E1 contain one or more regions deletions selected from the location between the at aa 170-190, aa 260-290 or aa 330-380; and the expression vector is preferably a vaccinia viral vector. Ralston et al. teach that the recombinant vaccinia vector comprises the HCV envelope protein sequence, which is inherently expressed under the vaccinia viral promoter control and the HCV envelope protein sequence is also inherently operably linked to a 5-terminal ATG codon and a 3'-terminal codon (See pages 9-11 and pages 19-21). Ralston et al. do not teach which particular vaccinia viral vector is used.

9. Targilia et al. teach that the avipox virus canarypox (ALVAC) is a highly attenuated avian vaccinia virus with following characteristics: (a) no detectable duration or ulceration at the site of inoculation on rabbit skin; (b) rapid clearance of infection from the intradermal inoculation site on rabbit skin; (c) absence of any testicular inflammation in nude mice; (d) greatly reduced virulence as demonstrated by the results of intracranial challenge of both 3-week-old or newborn mice; (e) greatly reduced pathogenicity and failure to disseminate in immunodeficient (nude or cyclophosphamide treated) mice; and (f) dramatically reduced ability to replicate on a variety of human tissue culture cells. Despite these highly attenuated characteristics, the vector made by NYVAC strain retains the ability to induce strong immune responses to extrinsic antigens (See abstract).

10. Sutter et al. teach that the modified vaccina Ankara (MVA) is also a highly attenuated vaccinia virus that has been safety tested in human. It is approved that said virus is valuable for using as an efficient and exceptional safe vector to express any heterologous gene that it carries (See abstract).

11. Vanderbroeck et al. teach a method about how to use a factor-Xa cleavage site and histidine tag sequence as a fusion tag for expressing a fusion protein by constructing said tag sequences into an expression vector. The fusion protein containing both or one of the tags can be

more easily identified and efficiently purified by a commercial chromolgraphic procedure. Vanderbroeck et al. also disclose to use 6 histidine codons as fusion tag in the construct (See Abstract and Materials and Methods disclosed on pages 45-47).

12. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited references and combine the methods taught by Hsu et al. Ralston et al. Tartaglia et al. or. Sutter et al. and further in view of the teaching by Vanderbroeck et al. to use a particular vaccinia virus, such as the ALVAC vector taught by Tartaglia et al. or MVA taught by Sutter et al, for constructing an expressing viral vector to express the particular HCV envelope E1 fragment as a fusion protein with fusion tag disclosed by Vanderbroeck et al. in order to facilitate a more efficient expression and easy purification processes. Therefore, the claimed invention as a whole is prima facie obvious absence unexpected results to the contrary.

Conclusion

Claims 95-97 are free of the rejection. However, they are not in condition for allowance because they depend on the rejected claims.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Baoqun Li

Bao Qun Li
1/20/2006

/BAOQUN LI, MD/
PATENT EXAMINER